

Translation

PATENT COOPERATION TREATY

PCT/FR2003/001328



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BIF023280/GP	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR2003/001328	International filing date (day/month/year) 28 avril 2003 (28.04.2003)	Priority date (day/month/year) 30 avril 2002 (30.04.2002)
International Patent Classification (IPC) or national classification and IPC C12N 7/00		
Applicant INSTITUT PASTEUR		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet. <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items: I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 28 novembre 2003 (28.11.2003)	Date of completion of this report 03 September 2004 (03.09.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone N .

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I. Basis of the report

1. With regard to the elements of the international application:*

- ☐ the international application as originally filed
- ☒ the description:
 pages _____ 1-44 _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☒ the claims:
 pages _____ 1-52 _____, as originally filed
 pages _____, as amended (together with any statement under Article 19
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☒ the drawings:
 pages _____ 1/5-5/5 _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 38-42, 44-46

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 38-42, 44-46
are so unclear that no meaningful opinion could be formed (*specify*):

See the separate sheet

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1,2,24,38-42,44-46,48-52

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.

Claims 38-42 and 44-46 relate to a method for obtaining polynucleotides of interest including at least one D-base, using a Cyanophage S-2L polypeptide defined in terms of a desirable feature or property, namely that said Cyanophage S-2L polypeptide is "involved in D-base synthesis or is capable of causing, in a host micro-organism, the synthesis of at least one D-base". Such a formulation does not fulfil the requirement of clarity of PCT Article 5 (PCT Guidelines, III-4.7).

The substantive examination is restricted to the subject matter for which the application appears to provide support under the terms of PCT Article 6 and a disclosure under the terms of PCT Article 5, i.e. those parts of the claims that relate to a Cyanophage S-2L nucleotide sequence coding for a succinyladenylate synthetase defined, e.g., by SEQ ID NO: 175 (Table 1) or as described on page 43, line 28 to page 44, line 2.

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

1.1. The different inventions are as follows:

Invention 1: the nucleotide sequence of Cyanophage S-2L, characterised in that it corresponds to SEQ ID NO: 1 (claims 1, 49-52 (all in full), 2, 24, 48 (all in part)).

Inventions 2-527: nucleotide sequence coding for a Cyanophage S-2L polypeptide of SEQ ID NO: 2-527 (claims 2-37, 48 (all in part, insofar as they are applicable).

Invention 528: method for obtaining D-bases using Cyanophage S-2L (claims 38-41, 45 (all in part), 43, 47 (all in full)).

Invention 529: method for obtaining polynucleotides of interest including at least one D-base using Cyanophage S-2L (claims 38-41, 45 (all in part), 42, 44, 46 (all in full)).

1.2. These inventions are not so linked as to form a single general inventive concept (PCT Rule 13.1) for the following reasons:

The prior art describes the identification of Cyanophage S-2L and the composition of the DNA thereof, incorporating the D-base (2,6, diaminopurine) instead of the A-base (adenine) (Khudyakov et al, 1977, Kirnos et al, 1977 and Khudyakov et al, 1978, cited on page 3 of the description). These documents disclose that infection with Cyanophage S-2L induces new pathways for synthesising the modified A-bases in cyanobacteria, which

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

indicates the existence of viral genes involved in the synthesis of modified A-bases. The general concept, the synthesis of D-bases in cells infected by Cyanophage S-2L, is not novel and cannot constitute a single general inventive concept common to the plurality of subjects. Moreover, a person skilled in the art can arrive in an obvious manner at the nucleotide sequence of the genome of a known organism, in this case Cyanophage S-2L, by routine experimentation, without an inventive step being involved. Consequently, the genome nucleotide sequence, the reading frames of each of the Cyanophage S-2L polypeptides and the methods for obtaining D-bases or polynucleotides of interest including at least one D-base using Cyanophage S-2L, are not so linked as to form a single general inventive concept.

In order to move forward with the procedure and despite the lack of unity of invention, a substantive examination was carried out for the two inventions that have been searched (1 and 529).

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	1, 2, 24, 38-42, 44-46, 48-52	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1, 2, 24, 38-42, 44-46, 48-52	NO
Industrial applicability (IA)	Claims	1, 2, 24, 38-42, 44-46, 48-52	YES
	Claims		NO

2. Citations and explanations**2. Reference is made to the following documents:**

D1: KIRNOS M D ET AL: "2 AMINO ADENINE IS AN ADENINE SUBSTITUTING FOR A BASE IN S-2L CYANOPHAGE DNA" NATURE (LONDON), vol. 270, no. 5635, 1977, pages 369-370, XP0002239457 ISSN: 0028-0836, cited in the application

D2: KHUDYAKOV I YA ET AL: "2 6 DI AMINO PURINE A NEW ADENINE REPLACING BASE IN THE DNA OF CYANO PHAGE S-2" DOKLADY BIOCHEMISTRY (ENGLISH TRANSLATION OF DOKLADY AKADEMII NAUK, vol. 232, no. 1-6, 1977, pages 42-45, XP0008016379 1977 ISSN: 0012-4958, cited in the application

D3: KHUDYAKOV I YA ET AL: "CYANOPHAGE S-2L CONTAINS DNA WITH 2 6 DI AMINO PURINE SUBSTITUTED FOR ADENINE" VIROLOGY, vol. 88, no. 1, 1978, pages 8-18, XP008016377 EN ISSN: 0042-6822, cited in the application.

3. Invention 1 (claims 1, 2, 24, 48-52):**Novelty**

The genome nucleotide sequence of Cyanophage S-2L corresponding to SEQ ID NO: 1 is novel because it has not been disclosed in the prior art. Consequently, claims 1, 2, 24 and 48-52 are novel (PCT Article 33(2)).

Inventive step

Providing the genome sequence SEQ ID NO: 1 derived from the genome library of Cyanophage S-2L deposited at the CNCM under the reference I-2619, is not considered to be inventive, since a person skilled in the art can arrive in an obvious manner at the nucleotide sequence of a known organism, in the present case Cyanophage S-2L (D1-D3), via routine experimentation without an inventive step being involved.

Claims 1, 2, 24 and 48-52 do not involve an inventive step (PCT Article 33(3)).

4. Invention 529 (claims 38-42 and 44-46)**Novelty**

The prior art does not disclose a method for obtaining polynucleotides of interest including at least one D-base using a nucleotide sequence of Cyanophage S-2L coding for a succinyladenylate synthetase defined by SEQ ID NO: 175 (Table 1) or as described on page 43, line 28 to page 44, line 2. Consequently, the subject matter of claims 38-42 and 44-46 is considered to be novel (PCT Article 33(2)).

Inventive step

The present application claims a method for obtaining polynucleotides of interest including at least one D-base using a nucleotide sequence of Cyanophage S-2L coding for a succinyladenylate synthetase, but the effect of using said polynucleotide sequence in said method has not been shown. It appears that the actual invention, the identification of all the polynucleotide sequences required for obtaining polynucleotides of interest including at least one D-base, remains to be achieved.

Therefore, the subject matter of claims 38-42 and 44-46 does not involve an inventive step (PCT Article 33(3)).

PCT Articles 5 and 6

The subject matter of claims 38-42 and 44-46 is a method for obtaining polynucleotides of interest including at least one D-base using a nucleotide sequence of Cyanophage S-2L coding for a succinyladenylate synthetase defined by SEQ ID NO: 175 (Table 1) or as described on page 43, line 28 to page 44, line 2.

However, the application only discloses one example showing the expression of the gene coding for a Cyanophage S-2L succinyladenylate synthetase in *Escherichia coli*, without providing any evidence of the production of polynucleotides of interest including at least one D-base in these transformed bacteria. The effect of introducing the succinyladenylate synthetase gene in the D-base biosynthesis pathway in the transformed bacteria has not been shown and it appears that several genes of Cyanophage S-2L are necessary to obtain the polynucleotides of interest including at least one D-base, as suggested on

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page 43 (lines 12-20) of the description of the present application.

Consequently, the present application does not set forth the essential features for carrying out the invention to which claims 38-42 and 44-46 are directed, and in a sufficiently clear manner for a person skilled in the art to carry out the invention without undue effort and without exercising an inventive skill. Said claims cannot consequently be considered to be supported under the terms of PCT Article 6 and the application does not provide sufficient disclosure of the invention under the terms of PCT Article 5.